Remarks

This Amendment is submitted in response to the office action mailed December 14, 2006, in connection with the above-identified application (hereinafter the "Office Action"). The Office Action established a three-month period to respond expiring March 14, 2007. Accordingly, this Amendment is timely submitted.

Claims 1, 32, 34 through 37 are currently pending. Applicants respectfully request entry of new Claim 38. No new matter is introduced by Claim 38.

Rejections under 35 U.S.C. § 103(a)

Claims 1, 32, 34 through 37 are rejected under 35 U.S.C. § 103(a) as being unpatentable over *Preparation of aqueous polymeric nanodispersions by a reversible salting-out process: influence of process parameters on particle size* to Allémann et al. (hereinafter "*Allémann*") of record in combination with U.S. Patent No. 5,651,983 (hereinafter "*Kelm*").

Allémann discloses a process of preparation of polymeric nanodispersions containing polyvinyl alcohol and Eudragit S or ethyl acetate as stated in the Office Action. The Office Action further notes that *Allémann* teaches that these nanospheres are for sustained release dosage forms and therefore, it would have been prima facie obvious to one of ordinary skill in the art to use *Allémann*'s nanosphere dispersions for the water insoluble drugs with a reasonable expectation of success. Also, the Office Action points out that *Allémann* lacks the teaching of polyvinyl acetate phthalate instead of Eudragit. The Office Action relies on *Kelm* for this teaching.

Applicants respectfully submit that a *prima facie* case of obviousness has not been established. A key requirement to establish obviousness is some suggestion or motivation to modify the references or combine the teachings. What the combination of *Allémann* and *Kelm* lacks is any suggestion or motivation to combine.

First, as pointed out by the Examiner, *Allémann* discloses that nanospheres can be used for a sustained release dosage form. However, on page 253 of the paper, the document states, "Moreover, the results with the biocompatible poly(dl-lactic acid) should permit the use of this process for *injectable* sustained release dosage forms and for drug targeting" (italics added). Thus, the only route of administration specifically mentioned is a parenteral route. In contrast, the present invention focuses on an oral route of administration.

Turning to *Kelm*, this paper specifically discusses an oral route of administration. It fails to mention a parenteral route, so one of ordinary skill in the art would not be motivated to combine *Allémann* concerning a parenteral route with *Kelm* concerning an oral route.

Furthermore, *Kelm* specifically writes, "The dosage forms of the present invention are to be distinguished from controlled (sustained) release compositions which slowly release a drug active over an extended period of time and extend the drug action over that achieved with conventional delivery." (Column 4, lines 65:end to Column 5, lines 1:4). This passage would discourage a combination of the two references.

Moreoever, the present invention features an insoluble active agent. *Kelm* features bisacodyl. While bisacodyl is an insoluble active agent, the specific form of bisacodyl used in *Kelm* is a "rapidly dissolving bisacodyl" – "a physical form or composition which enhances the rate of dissolution of bisacodyl in the intestinal juices in the lumen of the colon compared to conventional bisacodyl formulations." (Column 5, lines 39:42). Thus, this rapidly dissolving bisacodyl can be arguably be considered soluble, and thus not an insoluble active agent as required in the present invention.

Kelm further states "the rapidly dissolving bisacodyl is selected from the group consisting of "micronized bisacodyl, inclusion complex of bisacodyl and a cyclodextrin, solid dispersion of bisacodyl on a hydrophilic substrate, commercially available bisacodyl powder, and any of the preceding solids or solid composing suspended in a self-emulsifying lipid vehicle." (Column 5, lines 59:67). The only form of the foregoing that speaks to a suspension is the solids in the self-emulsifying lipid vehicle. In contrast, *Allémann* is teaching aqueous suspensions.

Finally, the particle sizes of the composition in *Kelm* are not nanoparticles as taught in *Allémann*. In Column 4, lines 56:64, it is stated that the rapidly dissolving bisacodyl is preferably coated on the surface of or incorporated into substrates having a diameter of about 3 mm. This is significantly larger than the nanoparticles of *Allémann*.

Thus for the above foregoing reasons, there is no motivation to combine *Allémann* with *Kelm* thereby unfulfilling the requirements of *a prima facie case* of obviousness.

The same claims are also rejected under 35 U.S.C. § 103(a) as being unpatentable over *Allémann* in combination with U.S. Patent No. 4,343,789 to Kawata (hereinafter "*Kawata*"), or U.S. Patent No. 4,895,725 to Kantor (hereinafter "*Kantor*") by themselves or in combination further in view of *Kelm*. The Office action states "What is lacking in Kawata or Kantor is the teaching of polyvinyl acetate phthalate." As discussed above, *Kelm* should not be combined with *Allémann* for a teaching regarding the use of polyvinyl acetate phthalate. Thus, as with the prior rejection, a prima facie case of obviousness has not been established.

Thus, in view of the foregoing arguments, Applicants respectfully request reconsideration of the present application. If a telephone interview would be of assistance in advancing the

prosecution of this application, Applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

Respectfully submitted,

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